# Advances in Hydroboration:
# Metal-Free Oxygen-Directed Hydroboration
# and
# Asymmetric Hydroboration with *N*-tosyl-(*R*,*R*)-2,6-diisopropyl-1,4-borazinane

by

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In Memory of my Grandparents:

Frederick John Rarig, Sr.
&
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ABSTRACT

Advances in Hydroboration:
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Chair: Edwin Vedejs

The work described herein addresses two unresolved issues in the hydroboration literature: 1) The regioselective hydroboration of 1,2-disubstituted olefins, and 2) the asymmetric hydroboration of prochiral olefins.

Metal-free oxygen-directed hydroboration of 1,2-disubstituted olefins in homoallylic alcohols, lithium alkoxides, and ethers has been achieved using triflic acid-activated dimethylsulfide·borane conditions building on previous work in the Vedejs group involving homoallylic amine-directed hydroboration. Optimization has led to a pre-activation approach to generate $TfOBH_2$ that provides 1,3-diols from alcohols and alkoxides with excellent regioselectivity (>20:1) upon oxidative workup. An *in situ* approach to $TfOBH_2$ provides optimal results in the case of homoallylic ethers, including allyl ethers, which afford monoprotected 1,3-diols upon oxidative workup. The originally envisioned mechanistic pathway for these transformations, in which the

generation of a $TfOBH_2$-oxygen complex enables intramolecular $S_N2$-like boron-alkene complexation, can account for the regioselectivity, and the observation that homoallylic alcohols are preferentially hydroborated in the presence of excess cyclohexene is consistent with this mechanism. However, diastereoselectivity remains elusive, indicating that the mechanism of oxygen-directed hydroboration (ODHB) is not straightforward. Mechanistic studies have provided little insight into the pathway(s) leading to the regioselective, yet non-diastereoselective transformations. Oxygen-directed hydroboration remains an enigmatic phenomenon, in general.

*N*-Tosyl-(*R*,*R*)-2,6-diisopropyl-1,4-borazinane, the first C*2*-symmetric borane incorporated into a 2,6-disubstituted-six-membered boracycle, has been generated in pursuit of an asymmetric hydroborating reagent that is capable of achieving excellent enantioselectivity on all four types of prochiral alkenes. Masamune's (*R*,*R*)-2,5-dimethylborolane is the single most versatile asymmetric hydroborating agent in the literature, and serves as both inspiration and measuring stick for this work. The synthesis of *N*-tosyl-(*R*,*R*)-2,6-diisopropyl-1,4-borazinane is streamlined compared with the preparation of Masamune's borolane, thanks to diastereoselective boracycle formation, successful resolution of *trans*-borazinane enantiomers via alanine complexation/crystallization, and a one-pot hydroboration procedure from the diastereo-enriched alanine complex. On the other hand, *N*-tosyl-(*R*,*R*)-2,6-diisopropyl-1,4-borazinane only achieves good enantioselectivity (86% ee) with *cis*-1,2-disubstituted (Type II) alkenes. This is more reminiscent of Brown's diisopinocampheylborane than of Masamune's borolane, which provides superior enantioselectivity with *cis*- and *trans*-1,2-disubstitued (Type II and III) and trisubstituted (Type IV) alkenes.